

Appl. No. 09/887,208  
Amdt. dated Dec. 22, 2003  
Reply to Office Action of June 20, 2003

**In the Claims:**

Please amend claims 43-86 and add new claims 87-114.

**Listing of Claims:**

43. (Currently amended) A method for selectively removing at least one biological contaminant from a selected compound, the method comprising:

(a) directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound, so as to flow along a first selective membrane;

(b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

(c) applying at least one voltage potential across each of the first and second fluid streams, wherein the application of such voltage potential causes movement of whereby at least a portion of a selected one of the at least one biological contaminant and the selected compound ~~though moves through~~ the first selective membrane into the second fluid stream such that the other of the at least one biological contaminant and the selected compound is substantially prevented from entering the second fluid stream, and ~~wherein whereby~~ substantially all transmembrane migration of the selected one of the at least one biological contaminant and the compound is initiated by the application of the voltage potential; and

(d) maintaining step (c) until at least one of the fluid streams contains the desired purity of the compound.

44. (Currently amended) The method according to claim 43 further comprising:  
directing a third fluid stream separated from a selected one of the first and second fluid streams by a second selective membrane;

applying concurrently the voltage potential across the third fluid stream so as to cause migration of at least a portion of at least one of the compound and the biological contaminants into the third fluid stream;

directing a fourth fluid stream separating from the other of the first and second fluid streams by a third selective membrane; and

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applying concurrently the voltage potential across the fourth fluid stream ~~so as to cause migration of whereby~~ at least a portion of at least one of the compound and the biological ~~contaminants~~contaminant moves into the fourth fluid stream, and whereby substantially all transmembrane migration of the selected one of the at least one biological contaminant and the compound is initiated by the application of the voltage potential.

45. (Currently amended) The method according to claim 43 ~~wherein the method further comprises~~comprising periodically stopping and reversing the voltage potential to cause movement of at least any components of the first fluid stream having entered the selective membrane to move back into the first fluid stream and ~~wherein whereby~~ substantially not causing any of selected one of the biological ~~contaminants~~contaminant and the compounds that have entered the second fluid stream to re-enter the first fluid stream.

46. (Currently amended) The method according to claim 43 ~~wherein whereby~~ the compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.

47. (Currently amended) The method according to claim 43 ~~wherein whereby~~ the biological contaminant is selected from the group consisting of viruses, bacteria, prions, yeast, lipopolysaccharides, toxins, endotoxins, and combinations thereof.

48. (Currently amended) The method according to claim 43 ~~wherein whereby~~ step (d) results in the compound being substantially free of biological contaminants.

49. (Currently amended) A method for concurrently isolating both a selected compound and at least one biological contaminant from a fluid stream, the method comprising:

- (a) directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound, so as to flow along a first selective membrane;
- (b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

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- (c) directing a third fluid stream separated from the first fluid stream by a second selective membrane;
- (d) applying concurrently at least one voltage potential across each of the first, second and third fluid streams, wherein the application of such voltage potential causes movement of whereby at least the selected compound ~~though moves through~~ the first selective membrane into the second fluid stream such that at least a portion of the biological contaminant is prevented from entering the second fluid stream and ~~causes movement of~~ at least a portion ~~of~~ the biological contaminant remaining in the first fluid stream ~~moves~~ through the second selective membrane into the third fluid stream, and ~~whereby substantially all transmembrane migration of the selected one of the at least one biological contaminant and the compound is initiated by the application of the voltage potential;~~ and
- (e) maintaining step (d) until at least one of the fluid stream contains the desired purity of the selected compound.

50. (Currently amended) The method according to claim 49 wherein the method further comprises comprising directing a fourth fluid stream separated from the second fluid stream by a third selective membrane and concurrently applying the voltage potential across the fourth fluid stream so as to cause the selective migration of at least one of any biological contaminants ~~contaminant which have has~~ entered the second fluid stream and other components in the second fluid stream through the third selective membrane into the fourth fluid stream.

51. (Currently amended) The method according to claim 49 wherein the method further comprises comprising periodically stopping and reversing the voltage potential to cause movement of at least any components of the first fluid stream having entered the first selective membrane to move back into the first fluid stream and ~~wherein whereby~~ substantially not causing any of the selected compound that has entered the second fluid stream to re-enter the first fluid stream.

52. (Currently amended) The method according to claim 49 wherein ~~wherein whereby~~ the first fluid stream further includes a compound from which the selected compound is separated, ~~wherein whereby~~ such compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.

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53. (Currently amended) The method according to claim 49 ~~wherein~~whereby the biological contaminant is selected from the group consisting of viruses, bacteria, prions, yeast, lipopolysaccharides, toxins, endotoxins, and combinations thereof.

54. (Currently amended) The method according to claim 49 ~~wherein~~whereby the pH of the first fluid stream is selected by-selectively adding a buffer having the required pH.

55. (Currently amended) The method according to claim 52 ~~wherein~~whereby the first fluid stream has a pH selected ~~at one from the group consisting of~~ a pH lower than the isoelectric point of the compound, a pH about the isoelectric point of the compound, and a pH higher than the isoelectric point of the compound.

56. (Currently amended) The method according to claim 49 ~~wherein~~whereby the first selective membrane has a molecular mass cut-off of at least about 3 kDa.

57. (Currently amended) A method for ~~concurrently~~ isolating both a selected compound and at least one biological contaminant from a fluid stream, the method comprising:

- (a) directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound so as to flow along a first selective membrane;
- (b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;
- (c) directing a third fluid stream separated from the second fluid stream by a second selective membrane;
- (d) applying concurrently at least one voltage potential across each of the first, second and third fluid streams, ~~wherein the application of such voltage potential causes movement of~~whereby at least one of the selected compound and biological contaminant ~~through~~moves through the first selective membrane into the second fluid stream and causes selected migration of at least a portion of at least one of the selected compound and the biological contaminant having entered the second fluid stream through the second selective membrane into the third fluid stream, and whereby substantially all transmembrane migration of the selected one of the at least one biological contaminant and the compound is initiated by the application of the voltage potential; and

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(e) maintaining step (d) until at least one of the fluid stream contains the desired purity of the selected compound.

58. (Currently amended) The method according to claim 57 wherein the method further comprises comprising directing a fourth fluid stream separated from the first fluid stream by a third selective membrane and concurrently applying the voltage potential across a fourth fluid stream so as to cause selective migration of at least one of any biological contaminants which have remained in the first fluid stream and any other components in the first fluid stream through the third selective membrane into the fourth fluid stream.

59. (Currently amended) The method according to claim 57 wherein the method further comprises comprising periodically stopping and reversing the voltage potential to cause movement of any components of the first fluid stream having entered the first selective membrane to move back into the first fluid stream and wherein whereby substantially not causing any of the selected compound and biological contaminant that have entered the second fluid stream to re-enter the first fluid stream.

60. (Currently amended) The method according to claim 57 wherein whereby the first fluid stream further includes a compound from which the selected compound is separated, wherein whereby such compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.

61. (Currently amended) The method according to claim 57 wherein whereby the biological contaminant is selected from the group consisting of viruses, bacteria, prions, yeast, lipopolysaccharides, toxins, endotoxins, and combinations thereof.

62. (Currently amended) The method according to claim 57 wherein whereby the pH of the first fluid stream is selected by selectively adding a buffer having the required pH.

63. (Currently amended) The method according to claim 60 wherein whereby the first fluid stream has a pH selected at-one from the group consisting of a pH lower than the isoelectric

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point of the compound, a pH about the isoelectric point of the compound, and a pH higher than the isoelectric point of the compound.

64. (Currently amended) The method according to claim 57 wherein whereby the first selective membrane has a molecular mass cut-off of at least about 3 kDa.

65. (Currently amended) A method for concurrently isolating both a selected compound and at least one biological contaminant from a fluid stream, ~~the method comprising:~~

- (a) directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound so as to flow along a first selective membrane;
- (b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;
- (c) directing a third fluid stream separated from first fluid stream by a second selective membrane;
- (d) applying concurrently at least one voltage potential across each of the first, second and third fluid streams, ~~wherein the application of such voltage potential causes movement of~~ whereby at least a portion of the biological contaminant ~~though moves through~~ the first selective membrane into the second fluid stream such that at least a portion of the selected compound is prevented from entering the second fluid stream and ~~causes movement of~~ at least a portion of at least one of the selected compound and any biological contaminant remaining in the first fluid stream moves through the second selective membrane into the third fluid stream, and whereby substantially all transmembrane migration of the selected one of the at least one biological contaminant and the compound is initiated by the application of the voltage potential; and
- (e) maintaining step (d) until at least one of the fluid streams contain the desired purity of the selected compound.

66. (Currently amended) The method according to claim 65 wherein ~~the method further comprises~~ comprising directing a fourth fluid stream separated from the second fluid stream by a third selective membrane and concurrently applying the voltage potential across a fourth fluid stream so as

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to cause selected migration of at least a portion of any biological contaminants which have entered the second fluid stream through the third selective membrane and other components in the second fluid stream into the fourth fluid stream.

67. (Currently amended) The method according to claim 65 ~~wherein the method further comprises comprising~~ periodically stopping and reversing the voltage potential to cause movement of at least any components of the first fluid stream having entered the first selective membrane to move back into the first fluid stream and ~~wherein whereby~~ substantially not causing any of the biological contaminants that have entered the second fluid stream to re-enter the first fluid stream.

68. (Currently amended) The method according to claim 65 ~~wherein whereby~~ the first fluid stream further includes a compound from which the selected compound is separated, ~~wherein whereby~~ such compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.

69. (Currently amended) The method according to claim 65 ~~wherein whereby~~ the biological contaminant is selected from the group consisting of viruses, bacteria, prions, yeast, lipopolysaccharides, toxins, endotoxins, and combinations thereof.

70. (Currently amended) The method according to claim 65 ~~wherein whereby~~ the pH of the first fluid stream is selected by selectively adding a buffer having the required pH.

71. (Currently amended) The method according to claim 68 ~~wherein whereby~~ the first fluid stream has a pH selected ~~at one from the group consisting of~~ a pH lower than the isoelectric point of the compound, a pH about the isoelectric point of the compound, and a pH higher than the isoelectric point of the compound.

72. (Currently amended) The method according to claim 65 ~~wherein whereby~~ the first selective membrane has a molecular mass cut-off of at least about 3 kDa.

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73. (Currently amended) A system for selectively removing at least one biological contaminant from a selected compound, the system comprising:

means for directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound, so as to flow along a first selective membrane;

means for directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby; and

means for applying at least one voltage potential across each of the first and second fluid streams, wherein whereby the application of such voltage potential causes movement of a selected one of the at least a portion of the at least one biological contaminant and the selected compound through the first selective membrane into the second fluid stream such that the other of the at least one biological contaminant and the selected compound is substantially prevented from entering the second fluid stream, and wherein whereby substantially all transmembrane migration of the at least one biological contaminant is initiated by the application of the voltage potential.

74. (Currently amended) A system for ~~concurrently~~ isolating both a selected compound and at least one biological contaminant from a fluid stream, ~~the system~~ comprising:

means for directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound so as to flow along a first selective membrane;

means for directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

means for directing a third fluid stream separated from the first fluid stream by a second selective membrane; and

means for applying concurrently at least one voltage potential across each of the first, second and third fluid streams, wherein the application of such voltage potential causes movement of whereby the selected compound moves through the first selective membrane into the second fluid stream such that at least a portion of the biological contaminant is prevented from entering the second fluid stream, and causes movement of at least a portion the biological contaminant remaining in the first fluid stream moves through the second selective membrane into the third fluid stream, and whereby substantially all transmembrane migration of the selected one of the at least one biological contaminant and the compound is initiated by the application of the voltage potential.

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75. (Currently amended) The system according to claim 74 wherein the system further comprises comprising means for directing a fourth fluid stream separated from the second fluid stream by a third selective membrane and concurrently applying the voltage potential across the fourth fluid stream so as to cause the migration of any biological contaminants which have entered the second fluid stream through the third selective membrane into the fourth fluid stream.

76. (Currently amended) A system for concurrently isolating both a selected compound and at least one biological contaminant from a fluid stream, the system comprising:

means for directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound so as to flow along a first selective membrane;

means for directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

means for directing a third fluid stream separated from the second fluid stream by a second selective membrane; and

means for applying concurrently at least one voltage potential across each of the first, second and third fluid streams, wherein the application of such voltage potential causes movement of whereby the selected compound and biological contaminant though moves through the first selective membrane into the second fluid stream and causes movement of at least a portion of at least one of the selected compound and the biological contaminant having entered the second fluid stream moves through the second selective membrane into the third fluid stream, and, whereby substantially all transmembrane migration of the selected one of the at least one biological contaminant and the compound is initiated by the application of the voltage potential.

77. (Currently amended) The system according to claim 76 wherein the system further comprises comprising means for directing a fourth fluid stream separated from the first fluid stream by a third selective membrane and concurrently applying the voltage potential across a fourth fluid stream so as to cause the migration of any biological contaminants which have remained in the first fluid stream through the third selective membrane into the fourth fluid stream.

78. (Currently amended) A system for concurrently isolating both a selected compound and at least one biological contaminant from a fluid stream, the system comprising:

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means for directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound so as to flow along a first selective membrane;

means for directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

means for directing a third fluid stream separated from the first fluid stream by a second selective membrane; and

means for applying concurrently at least one voltage potential across each of the first, second and third fluid streams, ~~wherein the application of such voltage potential causes movement of~~ whereby at least a portion of the biological contaminant ~~though moves through~~ the first selective membrane into the second fluid stream such that at least a portion of the selected compound is prevented from entering the second fluid stream and ~~causes movement of~~ at least a portion of at least one of the selected compound and any biological contaminant remaining in the first fluid stream ~~moves through~~ the second selective membrane into the third fluid stream, and, whereby substantially all transmembrane migration of the selected one of the at least one biological contaminant and the compound is initiated by the application of the voltage potential.

79. (Currently amended) The system according to claim 78 wherein the system further comprises comprising means for directing a fourth fluid stream separated from the second fluid stream by a third selective membrane and concurrently applying the voltage potential across a fourth fluid stream so as to cause the migration of at least a portion of any biological contaminants which have entered the second fluid stream through the third selective membrane into the fourth fluid stream.

80. (New) A method of selectively removing a non-pathogenic biological contaminant from a mixture containing a compound and the contaminant comprising:

(a) placing the compound and contaminant mixture in a first solvent stream, the first solvent stream being separated from a second solvent stream by a selective membrane having a defined pore size;

(b) selecting a buffer for the first solvent stream having a required pH;

(c) applying an electric potential across the first and second solvent stream, whereby at least a portion of the compound moves through the membrane into the second solvent stream while

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the contaminant is substantially retained in the first solvent stream, and substantially all transmembrane migration of the compound is initiated by application of the electric potential;

(d) optionally, periodically stopping and reversing the electric potential whereby contaminants having entered the membrane move back into the first solvent stream, while compounds that have entered the second solvent stream do not re-enter the first solvent stream; and

(e) maintaining step (c), and optional step (d) if used, until the second solvent stream contains the desired purity of the compound.

81. (New) The method according to claim 80 whereby the compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.

82. (New) The method according to claim 80 whereby the contaminant is selected from the group consisting of non-pathogenic bacteria, non-pathogenic virus, lipopolysaccharide, toxin, endotoxin, and combinations thereof.

83. (New) The method according to claim 82 whereby the contaminant is a lipopolysaccharide.

84. (New) The method according to claim 82 whereby the contaminant is a toxin.

85. (New) The method according to claim 82 whereby the contaminant is an endotoxin.

86. (New) The method according to claim 80 whereby the solvent for the first solvent stream has a pH lower than the isoelectric point of the compound.

87. (New) The method according to claim 80 whereby the selective membrane has a molecular mass cut-off between about 3 kDa and about 80000 kDa.

88. (New) The method according to claim 80 whereby the electric potential is up to 300 volts.

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89. (New) The method according to claim 80 whereby the selective membrane has a molecular mass cut-off close to the apparent molecular mass of the compound.

90. (New) The method according to claim 80 whereby the solvent for the first solvent stream has a pH at about the isoelectric point of the compound.

91. (New) The method according to claim 80 whereby the solvent for the first solvent stream has a pH above the isoelectric point of the compound.

92. (New) The method according to claim 80 whereby the selective membrane has a molecular mass cut-off of at least about 3 kDa.

93. (New) The method according to claim 80 whereby the compound is collected or removed from the second solvent stream.

94. (New) The method according to claim 80 whereby the compound is substantially free of the contaminant.

95. (New) The method according to claim 80 further comprising the step of applying the electric potential across a third solvent stream, whereby the third solvent stream is separated from a selected one of the first and second solvent streams by a second selective membrane, and at least one of the compound and the contaminant moves through the second membrane and into the third solvent stream.

96. (New) The method according to claim 95 further comprising the step of applying the electric potential across a fourth solvent stream, whereby the fourth solvent stream is separated from the other of the first and second solvent streams by a third selective membrane, and at least a portion of at least one of the compound and the contaminant moves through the third membrane and into the fourth solvent stream.

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97. (New) A method of selectively removing a non-pathogenic biological contaminant from a mixture containing a compound and contaminant, comprising:

- (a) placing the compound and the contaminant mixture in a first solvent stream, the first solvent stream being separated from a second solvent stream by a selective membrane having a defined pore size;
- (b) selecting a buffer for the first solvent stream having a required pH;
- (c) applying an electric potential across the first and second solvent streams whereby at least a portion of the contaminant moves through the membrane into the second solvent stream while the compound is substantially retained in the first solvent stream, and substantially all transmembrane migration of the contaminant is initiated by application of the electric potential;
- (d) optionally, periodically stopping and reversing the electric potential whereby compound having entered the membrane moves back into the first solvent stream, while contaminants that have entered the second solvent stream do not re-enter the first solvent stream; and
- (e) maintaining step (c), and optional step (d) if used, until the first solvent stream contains the desired purity of the compound.

98. (New) The method according to claim 97 whereby the contaminant is selected from the group consisting of lipopolysaccharide, toxin, endotoxin, and combinations thereof.

99. (New) The method according to claim 97 whereby the contaminant is a lipopolysaccharide.

100. (New) The method according to claim 97 whereby the contaminant is a toxin.

101. (New) The method according to claim 97 whereby the contaminant is an endotoxin.

102. (New) The method according to claim 97 whereby the compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.

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103. (New) The method according to claim 97 whereby the solvent for the first solvent stream has a pH lower than the isoelectric point of the contaminant.

104. (New) The method according to claim 97 whereby the solvent for the first solvent stream has a pH at about the isoelectric point of the contaminant.

105. (New) The method according to claim 97 whereby the solvent for the first solvent stream has a pH above the isoelectric point of the contaminant.

106. (New) The method according to claim 97 whereby the selective membrane has a molecular mass cut-off close to the apparent molecular mass of the contaminant.

107. (New) The method according to claim 97 whereby the selective membrane has a molecular mass cut-off of at least about 3 kDa.

108. (New) The method according to claim 97 whereby the selective membrane has a molecular mass cut-off of between about 3 kDa and about 80000 kDa.

109. (New) The method according to claim 97 whereby the electric potential applied is up to about 300 volts.

110. (New) The method according to claim 97 whereby the contaminant is collected or removed from the second solvent stream.

111. (New) The method according to claim 97 whereby substantially all of the contaminant is removed from the mixture.

112. (New) The method according to claim 97 whereby the mixture comprises at least two types of contaminant and only one type is caused to move into the second solvent stream.

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113. (New) The method according to claim 97 further comprising the step of applying the electric potential across a third solvent stream, whereby the third solvent stream is separated from a selected one of the first and second solvent streams by a second selective membrane, and at least a portion of at least one of the compound and the contaminant moves through the second selective membrane and into the third solvent stream.

114. (New) The method according to claim 113 further comprising the step of applying the electric potential across a fourth solvent stream, whereby the fourth solvent stream is separated from the other of the first and second solvent streams by a third selective membrane, and at least a portion of at least one of the compound and the contaminant moves through the third selective membrane and into the fourth solvent stream.